

Cognitive Rehabilitation for Cognitive Dysfunction after Cancer and Cancer Treatment: Implications for Nursing Practice

Diane Von Ah, PhD, RN, Professor & Associate Dean of Academic Operations, Indiana
University School of Nursing, Indianapolis, IN

Adele Crouch, PhD candidate, RN, Indiana University School of Nursing, Indianapolis, IN

Address correspondence to Diane Von Ah, PhD, Professor & Associate Dean of Academic
Operations, Indiana University School of Nursing, 600 Barnhill Drive, Indianapolis, IN, 317-
278-2827, dvonah@iu.edu

Abstract

Objective: To provide an overview of cognitive rehabilitation approaches for cognitive
dysfunction after cancer and cancer treatment.

Data Sources: Review and synthesis of empirical articles.

Conclusion: Cognitive rehabilitation approaches, including cognitive behavioral therapy (CBT)
and cognitive training (CT), for cognitive dysfunction appear feasible to deliver, satisfactory to
participants, and have shown promising results in cancer survivors. Future research is needed to
address optimal dose, delivery method, access, cost and the vulnerable aging cancer survivor
population.

Implications for Nursing Practice: Oncology nurses must understand the available evidence and
be able to provide information and options to cancer survivors to address cognitive changes after
cancer.

Key Words: cognition, cognitive rehabilitation, cognitive training, and evidence-based practice,

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Background

Cancer survivors often incur a myriad of lingering symptoms after cancer and cancer treatment, including cognitive dysfunction.^{1,2} Cognitive dysfunction, defined as cognitive changes that negatively affect higher-order mental processes in one or more cognitive domains, including attention and concentration, learning and memory, information processing speed, visuospatial skill, language, and executive function,³ has been shown to be a prevalent, bothersome, and potentially debilitating symptom in a subset of cancer survivors.¹ Researchers have noted that cancer survivors with cognitive dysfunction also report decreased social interactions,⁴ poorer functional⁵ and work ability,⁶ as well as, overall poorer health-related quality of life.^{1,5,7}

Given the debilitating nature and potentially long-term adverse effects of cancer and cancer treatment-related cognitive dysfunction, identifying effective treatment options are necessary. Research in this area has been hampered by the lack of a clear etiology.¹ Underlying mechanisms of cognitive dysfunction in cancer survivors are unclear and most likely multifactorial.⁸⁻¹¹ However, health care providers, including advance practice nurses and nurse clinicians, have an obligation to understand the current evidence and options available to address cognitive dysfunction in cancer survivors.¹²

The National Comprehensive Cancer Network (NCCN) Survivorship Guidelines® provide information regarding the assessment, screening, and treatment of cognitive dysfunction.¹³ This guideline identifies cognitive rehabilitation as a first-line intervention to address cognitive dysfunction in cancer survivors. However, it stops short of defining or sharing the supporting evidence for its recommendations or the role nurses may have in developing and implementing these evidence based strategies.

Cognitive rehabilitation includes behavioral interventions that have been shown, to not only improve cognitive function, but also have included goal attainment behavior, self-efficacy, memory enhancement, and problem solving techniques in patients with traumatic brain injury.¹⁴ Cognitive rehabilitative approaches have included programs in ‘cognitive training’(CT) or ‘brain training’ and those that use ‘strategy training’ also known as ‘cognitive behavioral therapy’ (CBT) and could include psycho-educational approaches. Cognitive rehabilitation therapy has long been used to address cognitive dysfunction in individuals with cognitive injury.¹⁵ However, less is known regarding the efficacy of cognitive rehabilitation approaches (CBT and CT) in cancer survivors. Therefore, the purpose of this integrative review was to provide an overview of cognitive rehabilitation approaches for cognitive dysfunction after cancer and cancer treatment. In addition, the nurse’s role in addressing cognitive dysfunction in cancer survivors will be emphasized. Advance practice nurses and oncology nurse clinicians are often the first healthcare providers in which cancer survivors report cognitive changes, and; therefore, they must have the requisite information to support cancer survivors effectively and provide optimal care.¹²

Methods

The Whittemore and Knafl¹⁶ integrative review method was used to conduct the review and included problem identification, literature search, data evaluation, and graphic presentations. Databases searched were PubMed, Med line and PsychINFO. Search terms used were “cognitive impairment” OR “cognitive dysfunction” AND “cognitive rehabilitation” Or “cognitive training” AND “cancer” or “cancer survivor.” Search limitations were English language and publication year 2000 to March, 2019.

Inclusion criteria were peer-reviewed primary interventional research articles that included cognitive rehabilitation approaches for cancer survivors. Review articles were excluded,

but reference lists of relevant reviews were hand-searched for further citations. After reviewing article titles and abstracts and eliminating duplicate articles, full-text articles were obtained based on title and abstract evaluation, and criteria were applied to determine article eligibility. The studies selected for the review were limited to those empirical manuscripts that were in English and examined cognitive rehabilitative approaches to address cognitive dysfunction in adult cancer survivors. Cognitive impairment in pediatric patients were not addressed in this review due to the specificity of cognitive and development issues found in children.

Data was extracted from articles that met criteria. Data was reduced, grouped, and compared among articles. Articles were separated into the types of cognitive rehabilitation approaches used (CBT and CT) specific cognitive outcome measures were identified, results were condensed, and outcomes presented.

Results

A total of 1466 manuscripts were identified in the first initial search. Duplicate manuscripts and those that did not meet the inclusion criteria were not retained. A total of 27 manuscripts met the inclusion criteria and were identified for review and synthesis. Figure 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram.

Cognitive Rehabilitation Approaches

The 27 cognitive rehabilitation interventional studies that meet the eligibility criteria included a total of 1543 participants, who were predominately middle-aged (mid-fifties), highly educated and female breast cancer survivors. In fact, 12 or 46% of the studies included in this review focused solely on breast cancer survivors, and of those with mixed cancer diagnoses, most were breast cancer survivors. Intervention studies included randomized controlled trials

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(n=18), partially randomized, quasi or non-randomized controlled trials (n=3), single arm studies (n=5) and one retrospective assessment. Most of the research was limited by small samples (n<100) and inferior study designs (no control arm or waitlist/non-contact control arms versus attention control comparisons). Cognitive domains assessed in these studies included primarily memory, attention, speed of processing, and executive function, which is consistent with previous meta-analyses identifying these as areas of primary concern by cancer survivors with cognitive dysfunction.¹⁷⁻¹⁹

Table 1 displays the author, year published, cancer population (if known), design, type of cognitive rehabilitation approach, cognitive domains assessed, and cognitive outcomes.

Cognitive rehabilitative approaches included CBT with or without psychoeducational programs and CT approaches. The following section will provide an integrated summary of the cognitive rehabilitation approaches utilized in these studies and their outcomes.

Cognitive-Behavioral Training

CBT programs are designed to improve or restore mental function through behaviorally orientated programs that may include retraining of lost cognitive abilities and compensatory strategies or more inclusive behavioral programs such as social support and self-efficacy.²⁰

While CBT does not include cognitive behavioral psychotherapy, generally it does focus on eliminating negative thoughts and beliefs, establishing goals, developing problem solving skills and/or implementing new behaviors to cope with cognitive dysfunction. Activities can also include psychoeducation, relaxation and/or mindfulness strategies. These activities can be delivered in-person, over the telephone, via video conference, or the internet.²¹

Eleven studies were identified that focused on understanding the implications of CBT on cognitive dysfunction in cancer survivors.²²⁻³² The sample sizes in these studies were quite

small. In fact, in the 11 total trials, there were a total of 442 participants and no study had more than 100 participants. The composition of the participants varied with 6 studies offering the intervention to a mixed group of survivors,^{23,24,28,30-32} 4 to breast cancer survivors,^{25-27,29} and one study focusing primarily on brain tumor patients.²² Interventions focused on psychoeducation,²⁸⁻³⁰ self-efficacy,^{23,24,30} self-regulation,²⁵⁻²⁷ and mindfulness techniques.³² All of the studies included in this review found some positive cognitive intervention effects of CBT. The majority of the positive cognitive outcomes were noted in either subjective (self-report) or neurocognitive test performance, but often results were mixed or not sustained beyond initial post-treatment time frames (Refer to Table 1 for details). Only one early study with primary brain tumor patients noted improvements in independence and productivity which were objectively assessed by clinicians.²² The majority of the intervention studies were also identified to be satisfactory by participant reports.²⁶

Notably, work in this field has primarily been advanced by three distinct research groups who have conducted multiple studies (n=7 of the 11 studies) in the effort to test and/or enhance CBT programs to address cognitive dysfunction in cancer survivors.^{23-28,30} McDougall and colleagues²³ were the first to test the efficacy of a memory training and self-efficacy program in a large sample of elderly (n=78 with a subset of 11 cancer patients). These participants reported improvement in perceived cognitive function, memory efficacy and meta-memory (or perceived capability, self-awareness and strategies to aid memory). In a follow-up pilot study, these researchers found improvements in perceived cognitive function (memory ability), as well as, improvement in visual memory performance in the intervention group (n = 8) compared to controls (n = 14).²⁴ Ferguson and colleagues^{26,27,33} conducted the most studies in this area, completing three separate studies piloting the Memory Attention Adaptation Training (MAAT)

program, which included memory, attention and self-awareness training. In their first one-arm trial, improvement was noted in perceived cognitive function as well as objectively measured verbal memory, executive functioning and psychomotor performance.³³ In the 2012 follow-up randomized clinical trial, breast cancer survivors who were randomly assigned to the MAAT program (n = 19) demonstrated greater improvements in verbal memory compared to those in the waitlist control (n = 21).²⁶ However, in this follow-up study, no improvement was noted in perceived cognitive concerns. Finally, Ferguson and colleagues²⁷ tested the MAAT program delivered by video conferencing to breast cancer survivors. In this final pilot study, they found improvement in processing speed immediately post-intervention and improvement in perceived cognitive dysfunction at a 2-month follow-up compared to controls. However, there was no demonstrated improvement in memory at either time point. The authors identify that the MAAT training program could be delivered via video conferencing; thus, increasing access to rural survivors who are often unable to participate. However, this intervention unlike others required a licensed psychiatrist to perform the training adding cost concerns for under- or un-insured cancer survivors.²⁵⁻²⁷ The third research team conducted two CBT studies, which combined psychoeducation and problem-solving approaches to address cognitive dysfunction in a mixed group of cancer survivors. In the first trial by this team, Shuurs and Green²⁸ noted improvement in immediate and delayed memory and visuospatial skills for up to 3 months post-intervention. In a follow-up study, King and Green³⁰ used the same CBT program and failed to note significant improvements in memory, but did find improvements in perceived cognitive function and information processing speed for up to 3 months post-intervention, as well as, improved cognitive self-efficacy. The remaining studies used a combination of approaches including compensatory strategies, psychoeducation,²⁹ mindfulness,³² and one CBT study attempted to

ameliorate cancer-related fatigue as a mechanism to improve perceived cognitive function in cancer survivors³¹ with positive results (See Table 1).

Cognitive Training Programs for Cognitive Dysfunction

CT programs focus specifically on structured practice on cognitive tasks with the intent to improve and/or maintain cognitive function. Based on Hallock and colleagues³⁴, characteristics of cognitive training include repetitive, standardized, problem-orientated tasks that target specific cognitive domains to restore impaired skills. CT can be delivered on an individual basis or group setting and/or be computer assisted.

Sixteen studies (including 1101 cancer survivors) were found that focused primarily on the effects of CT to improve cognitive functioning in cancer patients. Becker and colleagues³⁵ combined computerized CT with 6-weekly group sessions to improve cognitive dysfunction (See Table 1). Participants in these training programs included breast cancer survivors (n= 7),³⁵⁻⁴¹ primary brain tumor patients (n=5),⁴²⁻⁴⁶ prostate cancer survivors (n=1),⁴⁷ and mixed cancer groups (n=3).^{14,48,49} The training programs differed in regards to content and length, but most of the programs focused on memory training, speed of processing or problem solving (executive functioning). Delivery method also varied among the studies with some providing individual training and others provided group sessions. Computerized CT programs were used in a number of studies, with 5 studies using the InSight program known now as BrainHQ from Posit Science®.^{6,14,35,41,47} See Table 1 for further descriptions.

In summary, the majority of CT programs reviewed noted improvements in subjective and/or objective cognitive performance on neurocognitive tests. In fact, all but one study noted intervention effects of CT. Poppelreuter and colleagues⁴⁸ were the only research team that did not find significant intervention effects in a mixed group of in-patient cancer rehabilitation

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patients; however results were hypothesized to have been confounded with overall recovery.

Overall, in the cognitive training studies reviewed, significant intervention effects (small to moderate effect sizes) were noted with CT. Positive intervention effects were noted primarily in the cognitive domains of memory (immediate and delayed recall) and speed of processing across these studies. Participants also identified their satisfaction with the CT programs.

Data Quality and Analysis

The level of evidence of the individual studies ranged from level II to level IV including well-designed RCTs to well-designed uncontrolled, case control or cohort studies.⁵⁰ Areas for improvement in future research include inclusion of attention control comparison, standardized assessment and definition of impairment (and thus, improvement) and addressing multiple outcome comparisons.

DISCUSSION

Implication for Research and Practice

Cognitive rehabilitation programs, including CBT and CT programs have been used to address cognitive dysfunction in cancer survivors. Positive intervention effects have been noted on both subjective (self-reported cognitive function) and objective (performance on neurocognitive tests) assessments. These findings suggest that, although more work is needed, cognitive rehabilitation may benefit cancer survivors with cognitive dysfunction.

CT, including computerized cognitive training programs, have been examined in more trials and with larger number of cancer survivors than other approaches. Based on the existing level of evidence, the Oncology Nursing Society has identified that cognitive training is 'likely to be effective' for addressing cognitive dysfunction in cancer survivors.⁵¹ These findings are encouraging, especially when combined with evidence from studies in the well elderly and other

chronic-illness populations ⁵²⁻⁵⁵ that suggest that cognitive training interventions promote neuroplasticity (form synaptic connections in response to learning) and may be beneficial. However, more research is warranted. There is a genuine need for larger, multi-site, pragmatic trials to fully understand the impact of CT. ^{56,57} Research to date has been conducted with small, single-center samples and studies with inferior designs (no control arm or no contact/waitlist controls versus attention control). In addition, more work is needed to understand the requisite dose and need for booster training for optimal treatment recommendations. As identified previously, although positive intervention effects were noted, they were often immediate and waned over time. Future research should address these unknown areas, validate its effectiveness and identify optimal treatment (dose) recommendations.

Overall, CBT, although tested in a smaller number of cancer survivors has shown promise as an option for addressing cognitive dysfunction after cancer and cancer treatment. Three main groups of researchers to date have been working to perfect programs to address cognitive concerns through psychoeducation, self-awareness, self-efficacy, and self-actualization methods. Similar to recommendations for CT, more research related to CBT is needed to establish it as an efficacious option for cancer survivors.

Future Considerations

Evidence based treatment options are needed to address the potentially debilitating effects of cognitive dysfunction after cancer treatment. Researchers and clinicians, including advance practice nurses and nurse clinicians, must consider important factors that will affect treatment effectiveness and uptake in the future. Three main issues that should be considered for the future in this area are cost, access, and vulnerable populations, such as our aging cancer population.

Cost and Access

Most of the CBT and CT interventions reported in this review were found to be feasible to recruit to, deliver and resulted in positive outcomes for cancer survivors; yet, few discussed the practical concerns of adopting and implementing these approaches on a larger scale. More research is needed regarding the access to and cost of these programs to deliver. Cancer and active cancer treatment already impact the cancer patient's ability to work ⁵⁸ and many experience long-term financial hardships. ⁵⁹ Programs developed to address cognitive dysfunction should be aimed at not only improving cognitive function, but also take into consideration their impact on work-related outcomes. In addition, the direct cost of participation (e.g. gas, transportation, etc.) and opportunity costs (e.g. time away from work/family) associated with participation in CBT or CT must be minimized. It is noteworthy that many of the participants in the studies reviewed were well-educated and most likely in a higher socioeconomic status. Cognitive rehabilitation programs must be designed and tested with a more diverse group of cancer survivors and must take into consideration both the direct and indirect costs of cognitive treatment. As noted in the study conducted by Cherrier and colleagues, ³² only 72% of the participants were able to attend all of the planned workshop sessions. These authors stressed more work is needed to enhance participation and address barriers, such as transportation costs to the center. ³² Ferguson and colleagues ²⁷ re-designed their MAAT program from an in-person format to be delivered via video conferencing and found positive results in both participant satisfaction and cognitive outcomes. However, this intervention required a licensed psychiatrist for delivery, which may ultimately, be a concern for broad scale dissemination for those who are under- or un-insured. Computerized CT programs are commercially available, and thus, readily accessible via the web and downloadable mobile

applications; but, again these programs come with a cost that currently is not offset by insurance. Future design and implementation of cognitive rehabilitation programs must consider both cost and access to be successfully integrated into survivorship care.

Vulnerable Population – Aging Cancer Survivors

As the nation ages and expected survival from cancer improves, approximately two-thirds of all cancer survivors will be aged 65 years and over by 2020.⁶⁰ This rapidly aging population represents a significant challenge in providing cancer care in the future. Older cancer survivors may be more susceptible to cognitive dysfunction as a result of lower cognitive reserve.⁶¹ In addition, family or informal caregivers may play an increased role for older survivors who often have more healthcare-related needs.⁶² Quality care of the older cancer survivor should include a thorough geriatric assessment.⁶³ The nursing assessment and survivorship treatment plan must incorporate outcomes especially germane to older cancer survivors, namely maintaining cognitive and physical functioning and preserving quality of life. Future cognitive rehabilitation programs must be developed and implemented that incorporate approaches amenable to the older cancer survivor and their families.

Conclusion

Cognitive rehabilitative approaches, including CBT and CT, may benefit cancer survivors with cognitive dysfunction. More research, including larger, multi-site pragmatic trials are needed that assess not only their effectiveness, but also the optimal dose, delivery, access, and cost of these programs. Advance practice nurses and nurse clinicians must play a crucial role in not only assessing for and identifying cognitive dysfunction in their patients, but also treating cognitive dysfunction, especially in the ever-increasing number of older cancer survivors. Routine assessments must include ruling out other treatable, confounding symptoms (depression,

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anxiety, and sleep disturbance), as well as, understanding the latest evidence regarding treatment options. Although more research is needed, cognitive rehabilitation has been identified as a first-line option by the NCCN, the Oncology Nursing Society, and more specifically, CT has demonstrated significant evidence for addressing cognitive dysfunction in cancer survivors.

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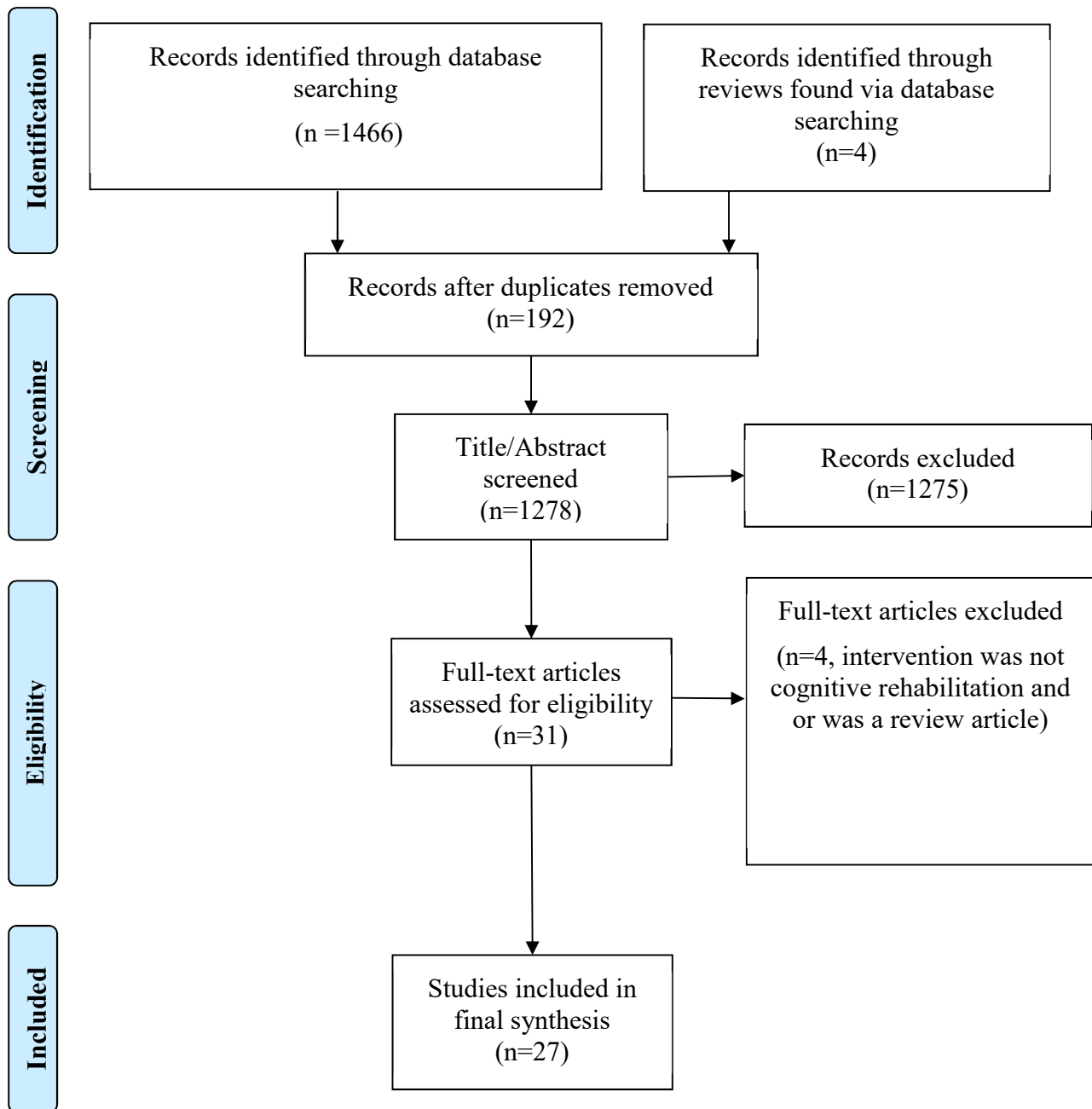


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram

Table 1 Cognitive Rehabilitation for Cognitive Dysfunction in Cancer Survivors

Author, year	Population	N	Study Design	Intervention	Primary Outcome	Results & Limitations
Sherer, et al., 1997 ²²	Brain tumor, post-acute	13	Retrospective review 1-16 months post-treatment	Cognitive rehabilitation: Content: Individualized therapy (speech, psych, occupational, vocational therapies, education)	Clinician ratings: <ul style="list-style-type: none"> Independence Productivity 	Independence: 6 (46%) patients increased independence during rehabilitation; 6 patients were unchanged; 1 decreased independence Productivity: 8 (62%) patients increased productivity; 4 were unchanged; 1 decreased Treatment gains were maintained 8 ± 7.6 months post-treatment Limitations: <ul style="list-style-type: none"> Retrospective review Small sample Ratings done by clinicians who treated patients
McDougall, et al., 2001 ²³	Cancer survivors, type not specified	78	RCT	Cognitive Rehabilitation: Content: Bandura's self-efficacy theory emphasized: 1. Health promotion 2. Everyday memory 3. Memory strategy use 4. Skill building through modeling techniques,	Subjective: Memory efficacy and metamemory Neurocognitive tests of memory	Improvements in subjective memory and memory self-efficacy. No improvement in objective memory performance. Limitations: <ul style="list-style-type: none"> Combined sample with chronic conditions, only 11 cancer patients Small sample Control – waitlist control

				<p>observing performance, developing awareness, handling mental challenges, and becoming more realistic & less fearful about cognitive aging.</p> <p>8 sessions of 1.25 hours each over 4 weeks.</p> <p>Control – waitlist control</p>		
Ferguson, et al., 2007 ²⁵	Breast cancer on average 8 years post-chemotherapy	29	<p>Pilot study, single arm</p> <p>Pre-test, 2- & 6-month post-tests</p>	<p>Cognitive rehabilitation: Memory & attention adaptation training (MAAT):</p> <p>Content: Education on memory, attention; Self-awareness training; Self-regulation training; Cognitive compensatory training</p> <p>4 individual monthly visits, 3 phone contacts, 30-50 min.</p>	<p>Subjective: perceived cognitive problems</p> <p>Neurocognitive tests of memory, attention, and executive function</p>	<p>Significant reduction in self-reported cognitive problems</p> <p>Verbal & executive function improved over baseline</p> <p>Limitations:</p> <ul style="list-style-type: none"> • Small sample • No control, single arm study • Mostly white, highly educated sample

Locke, et al., 2008 ⁴⁶	Primary brain tumor during radiation treatment	19 dyads	RCT	Cognitive Training: -Use of memory notebook/calendar -Use of problem solving techniques 6 (50 minute) sessions of each for 2 weeks	Subjective: Mood and quality of life Neurocognitive tests of immediate and delayed memory, language, attention, and visuo-construction completed at baseline only	Improvement in mood Intervention feasible and reported satisfaction Limitations: <ul style="list-style-type: none"> • Small sample • Control – no contact control, standard care • Failure to complete neurocognitive follow-up assessment to determine intervention effects
Gehring, et al., 2009 ⁴²	Low grade gliomas in remission	140	RCT	Combination: Cognitive retraining using a computer program (C-Car) plus Compensatory training consisting of six psycho-educational sessions on attention, memory, and executive function. 2hours/week for 6 weeks Control –waitlist control	Subjective: perceived cognitive complaints Neurocognitive tests of attention, memory, visual memory, working memory, verbal fluency, and executive function	Improvement in perceived cognitive function (reduced cognitive complaints) immediately and at 6 months post-intervention Improvement in attention and memory at 6 months post-intervention only Limitations: <ul style="list-style-type: none"> • Failure to account for confounding factors including tumor location, seizures, and current medications • Control – waitlist control
Poppelreuter, et al., 2009 ⁴⁸	Breast cancer patients, post-chemotherapy (in-patient)	96	Quasi-randomized control trial	Cognitive training: Group 1 - Strategies-group training in real life tasks and individualized; Group 2- computerized training,	Neurocognitive tests of attention, divided attention, working memory, and sustained memory	No Intervention effects Limitations: <ul style="list-style-type: none"> • The use of an inpatient setting may have affected the outcome. • Failure to address practice effects with repeated testing over time

				addressing attention and memory; vs. control 4-60 minute/ sessions/week		
Hassler, et al., 2010 ⁴³	High grade glioma	11	Pre, post-design	Cognitive Training - mnemonic training, with exercises to train perception, concentration, attention, memory, retentiveness, verbal memory, and creativity 2hrs per week, 6 weeks	Neurocognitive tests of attention, verbal memory, verbal memory (total learning), sustained attention, psychomotor speed, and verbal fluency	Improvement in verbal memory (total learning) No improvement in attention, verbal memory, sustained attention, psychomotor speed and verbal fluency Limitations: <ul style="list-style-type: none"> • Small sample • No control, single arm
McDougall, et al., 2011 ²⁴	Cancer survivors, mixed diagnosis, most breast cancer survivors	22	RCT	Cognitive rehabilitation: Memory training relaxation, a targeted memory topic, and practice. 8 sessions of memory training, including 20 minute relaxation, 30 minute practice Control - health training; frequency not provided.	Subjective: perceived meta-memory, memory self-efficacy Neurocognitive tests of memory – visual, verbal memory, global cognition, daily functioning	Improvement in memory confidence, greater capacity and decreased memory complaints. No neurocognitive improvement Visual memory improvement sustained over time and trends for improvement in verbal and global memory but not statistically significant. Limitations: <ul style="list-style-type: none"> • Small homogenous sample

				Booster sessions consisted of four weekly mandatory two-hour sessions over one month		
Von Ah, et al., 2012 ³⁶	Breast cancer survivors at least 12 months post-treatment	82	RCT	<p>Cognitive training – speed of processing training (ST) (InSight Program)</p> <p>Compensatory mnemonic memory training (MT)</p> <p>vs Waitlist control</p> <p>10 1-hour sessions over 8 weeks</p>	<p>Subjective: perceived cognitive function</p> <p>Neurocognitive tests of speed of processing and immediate, total and delayed memory</p>	<p>Improvement in subjective cognitive function in ST immediate and 2-months post-intervention and MT immediate post-intervention</p> <p>MT had improvement in immediate and delayed memory compared to waitlist control</p> <p>ST had improvement in immediate and delayed memory as well as processing speed compared to waitlist control immediate and 2 months post-intervention</p> <p>Limitations:</p> <ul style="list-style-type: none"> Control group-waitlist control No comparison between interventions
Ferguson, et al., 2012 ²⁶	Breast cancer survivors at least 18 months post-treatment	41	<p>RCT</p> <p>MAAT versus wait-list control</p> <p>Pre-test, post-treatment, 2-month follow-up</p>	<p>Cognitive rehabilitation, MAAT (see Ferguson, 2007)</p>	<p>Subjective: perceived cognitive function</p> <p>Neurocognitive tests of memory, executive function & processing speed</p>	<p>No improvement in self-reported cognitive function compared to control</p> <p>Significant improvement in memory (total recall) immediately and 2-months post-treatment</p> <p>Limitations:</p> <ul style="list-style-type: none"> Small sample, low power Control group-waitlist control
Ercoli, et al., 2013 ³⁷	Breast cancer survivors 18 months to 5 years post-treatment	27	<p>One group pre-test post-test design</p> <p>Pretest, end of treatment, 4 months post-treatment</p>	<p>Cognitive training:</p> <p>Content/Focus: attention, executive function, and memory challenges</p>	<p>Neurocognitive tests of verbal & visual memory, attention, executive and visuospatial functioning, and processing speed</p>	<p>Significant improvement in neurocognitive tests of memory and processing speed</p> <p>Effect size for change is moderate to high</p> <p>Intervention well tolerated</p> <p>Limitations:</p>

				<p>Training manual workbook with homework</p> <p>5-weekly group sessions, 2 hours long</p> <p>Intervention revision that reduced it from 6 to 5 sessions</p>		<ul style="list-style-type: none"> • Small sample • No control, single arm study
<p>Schuurs & Green, 2013²⁸</p>	<p>Cancer survivors, mix of diagnoses</p>	<p>54</p>	<p>Non-randomized; usual care comparison groups</p> <p>23 intervention; 9 cancer controls; 23 non-cancer controls</p> <p>Pretest, 6 weeks & 3 months after treatment</p>	<p>Cognitive rehabilitation:</p> <p>Content: strategy training, psychoeducation strategies targeting memory and attention, strategies targeting aging, health, & cognitive function; fatigue, sleep, and well being</p> <p>four 2-hour group sessions, between-session homework</p>	<p>Subjective: perceived cognitive function</p> <p>Neurocognitive tests of immediate memory, visuospatial, constructional, & delayed memory; visual attention & psychomotor speed</p>	<p>Improvement in perceived health-related quality of life immediate post and 3 months</p> <p>Improvement in perceived cognitive function over time.</p> <p>Improvement in immediate & delayed memory immediate and 3 months post intervention</p> <p>Improved visuospatial skills immediate and 3 months post-intervention</p> <p>Improvement in global cognition immediate and 3 months post-intervention</p> <p>Neurocognitive test results: 8 participants met reliable change criteria (36.4%); 1 cancer control had reliable improvement (12.5%); no non-cancer controls improved.</p> <p>Limitations:</p> <ul style="list-style-type: none"> • Non-random allocation • Assessors also conducted intervention
<p>Cherrier, et. al., 2013³²</p>	<p>Cancer survivors, mix diagnoses</p>	<p>28</p>	<p>RCT</p>	<p>Cognitive rehabilitation</p> <p>Content: memory aids (calendar, reminders etc.),</p>	<p>Subjective: perceived cognitive function</p> <p>Neurocognitive tests of memory, attention,</p>	<p>Improvement in self-reported cognitive impairment for intervention group</p> <p>Improvement in executive function (working memory); no improvement in memory</p>

				<p>use of memory skills (chunking, habit formation), mindfulness meditation</p> <p>Format: didactic, practice, review , homework</p> <p>Control: no intervention</p> <p>7 consecutive group sessions, 1 hour each</p>	<p>executive function, processing speed</p>	<p>Limitations:</p> <ul style="list-style-type: none"> • Small sample • No control for time & attention • No objective Screening for cognitive impairment • Intent-to-treat analysis was not used
Kesler, et al., 2013 ³⁹	Breast cancer at least 18 months post-chemotherapy	41	RCT	<p>Cognitive Training: 48 sessions that were 20-30 minutes long, involving combinations of 13 exercises to improve executive function</p>	<p>Subjective: perceived cognitive function</p> <p>Neurocognitive tests of memory, attention, executive function, cognitive flexibility, verbal fluency, letter fluency, processing speed</p>	<p>Improved perceived cognitive function (planning/organization and task monitoring)</p> <p>Improvement in cognitive flexibility, verbal fluency, letter fluency, and processing speed</p> <p>Limitations:</p> <ul style="list-style-type: none"> • Small sample
Miotto, et al., 2013 ⁴⁴	Primary brain tumor	21	Pre, post-design	<p>Cognitive Training: organizational strategy: organize, memorize, and retrieve words by category</p> <p>5 – 30 minute trials</p>	<p>Neurocognitive tests of verbal memory (word recall)</p> <p>Functional Magnetic Resonance Imaging (fMRI)</p>	<p>Improved verbal recall</p> <p>Increased activation on fMRI</p> <p>Limitations:</p> <ul style="list-style-type: none"> • Small sample • No control, single arm
Zucchella, et al., 2013 ⁴⁵	Primary brain tumor	53	RCT	<p>Cognitive Training: cognitive and metacognitive training</p>	<p>Neurocognitive tests – visual attention, immediate recall, delayed recall, verbal memory,</p>	<p>Improvement in visual attention and verbal memory</p> <p>Limitations:</p>

				16 1-hour sessions over 4 weeks	speed of processing, verbal fluency, language, non-verbal reasoning	<ul style="list-style-type: none"> • Small sample • Delivered during inpatient rehabilitation resulting in high costs of treatment
Goedendorp, et al., 2014 ³¹	Cancer survivors mixed cancer diagnoses primarily breast and testicular cancer – with fatigue	98	RCT	Cognitive Rehabilitation – Cognitive Behavioral Training focused on reducing fatigue 5-26 1-hour sessions Waitlist Control	Subjective: cognitive disability Neurocognitive test: reaction time/speed of information processing and attention and concentration	Improvement in subjective cognitive ability (less concentration problems and less disability) No improvement in neurocognitive tests Limitations: <ul style="list-style-type: none"> • Small sample • Control group-waitlist control
Ercoli et al., 2015 ³⁸	Breast cancer survivors 18 months – 5 years	48	RCT	See Ercoli, 2013	Subjective: cognitive complaints Neurocognitive tests: memory (total and delayed recall) executive function – cognitive flexibility, working memory, inhibition, complex reaction time, speed of processing, motor ability EEG	Improvement in subjective cognitive complaints Improvement in memory (total and delayed recall) at 2 months Limitations: <ul style="list-style-type: none"> • Small sample • Control group-waitlist control
King & Green, 2015 ³⁰	Mixed cancer diagnoses, predominately breast cancer survivors	45	RCT	Cognitive rehabilitation: Content: strategy training, psychoeducation strategies targeting memory and attention,	Subjective: perceived cognitive function Neurocognitive tests: memory (immediate and delayed), attention, executive function, processing speed, language, visuospatial	Improvement in perceived cognitive function in both groups over time. Improvement in speed of processing immediate post and 3 months post-intervention. Limitations: <ul style="list-style-type: none"> • Small sample

				<p>strategies targeting aging, health, & cognitive function; fatigue, sleep, and well being</p> <p>four 2-hour group sessions, between-session homework</p> <p>Control – waitlist control</p>	<p>skills, and global cognition</p>	<ul style="list-style-type: none"> Control group-waitlist control
Damholdt, et al., 2016 ⁴⁰	Breast cancer survivors	157	RCT	<p>Cognitive Training: computerized cognitive training - Happyneuron Pro, focus on attention, processing speed, learning memory, working memory, problem solving</p> <p>30 minutes/day, 5 days week for 6 weeks</p> <p>Control: waitlist control</p>	<p>Subjective: Perceived cognitive function</p> <p>Neurocognitive tests</p> <p>Working memory – primary outcome</p> <p>Verbal memory, learning, verbal fluency, attention, executive functioning – problem solving</p>	<p>No improvement of perceived cognitive function</p> <p>Improvement in verbal learning at 5 months and working memory post & 5 months post-intervention</p> <p>Limitations:</p> <ul style="list-style-type: none"> Small sample Control group-waitlist control
Ferguson, et al., 2016 ²⁷	Breast cancer survivors	47	RCT	<p>Cognitive Rehabilitation (See Ferguson et al., 2009)</p> <p>Control: attention control - supportive therapy</p>	<p>Subjective: Perceived cognitive function</p> <p>Neurocognitive tests: processing speed and verbal memory</p>	<p>Improvement in perceived cognitive function 2 months post-intervention</p> <p>Improvement in processing speed immediately post-intervention, no improvement in processing speed at follow-up and verbal memory at either time points</p> <p>Limitations:</p>

						<ul style="list-style-type: none"> Small sample
Park, et al., 2017 ²⁹	Breast cancer survivors	54	RCT	<p>Cognitive rehabilitation: promoting cognitive health, psychoeducation, self-awareness, strategies</p> <p>1-60minute in-person session + homework, 6 bi-weekly calls</p> <p>Control: Waitlist</p>	<p>Subjective: perceived cognitive function</p> <p>Neurocognitive tests: memory (immediate and delayed), attention, executive function- cognitive flexibility, working memory, verbal fluency in category, and verbal fluency in letter, processing speed, language</p>	<p>Improvement noted in perceived cognitive function</p> <p>Improvements noted in immediate memory, delayed memory, verbal fluency in category, and verbal fluency in letter</p> <p>Limitations:</p> <ul style="list-style-type: none"> Small sample Control – waitlist control
Bray, et al., 2017 ¹⁴	Mixed cancer group, mostly breast cancer survivors	242	RCT, pragmatic trial	<p>Cognitive Training- computerized including visual precision, divided attention, working memory, speed of processing (InSight Program)</p> <p>4 – 40minute per week for 15 weeks</p> <p>Control: standard care</p>	<p>Subjective: Perceived cognitive function</p> <p>Neurocognitive test – memory, attention, executive function- working memory, problem solving, & new learning, processing speed</p>	<p>Improvement in perceived cognitive function.</p> <p>No improvement noted on objective neurocognitive tests</p> <p>Limitations:</p> <ul style="list-style-type: none"> No blinding 14% enrolled did not complete the program
Becker, et al., 2017 ³⁵	Breast cancer survivors within 5 years of treatment	20	Pre-, post-treatment, Single arm	<p>Combination cognitive rehabilitation and cognitive training: psychoeducation, health promotion, computerized</p>	<p>Subjective: perceived cognitive concerns</p> <p>Neurocognitive tests: memory, executive function, processing speed, daily functioning</p>	<p>Improvement in perceived cognitive function (decreased self-report of cognitive concerns)</p> <p>Limitations:</p> <ul style="list-style-type: none"> Small sample No Control, single arm

				cognitive training (BrainHQ®) 6-90minute weekly in-person sessions + 45minute CT 3-4 times per week		
Wu, et al., 2018 ⁴⁷	Prostate	60	RCT	Cognitive training: BrainHQ® 40 1-hour session for 8 weeks Control: waitlist control	Neurocognitive tests: memory-verbal, visual, executive function – cognitive flexibility, attention, processing speed, motor ability	Improvement in processing speed immediately post and 2-months post-intervention Declined memory –verbal and visual memory immediately post-intervention Limitations: <ul style="list-style-type: none"> • Small sample • Control – waitlist control
Mihuta, et al., 2018 ⁴⁹	Mixed cancer group, majority breast cancer survivors	43	Partially randomized control trial	Cognitive training – 3 group 4weekly web-based Control – waitlist control & active community control	Subjective: perceived cognitive function Neurocognitive tests: memory, attention and concentration, executive function- working memory, impulsivity, processing speed	Improved perceived cognitive function post-intervention Improvement in attention at 3 months Limitations: <ul style="list-style-type: none"> • Small sample
Menses, et al., 2018 ⁴¹	Breast cancer survivors	60	RCT	Cognitive Training: BrainHQ® Control – No-contact control	Neurocognitive test: speed of processing and executive functioning	Improvement of speed of processing and executive functioning immediate, 6 weeks, and 6 months post-intervention Limitations: <ul style="list-style-type: none"> • Small sample • Control – no contact control

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